

Cooperative Catalysis by Indium and Palladium for the Allyl Cross-Coupling Reactions[†]

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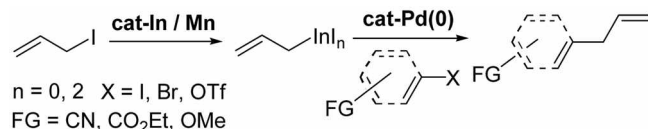
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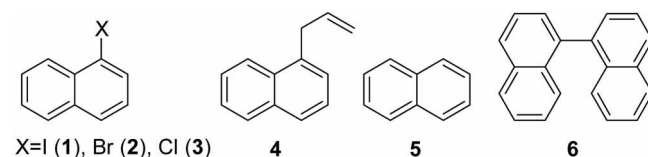
Key Words : Catalysis, Cross-coupling, Indium, Palladium, Manganese

Indium has emerged as useful metals in organic synthesis because of their intriguing chemical properties.¹ On the basis of these properties, a range of indium-mediated organic reactions have been found to be useful for organic reactions.² Generally, indium has been used in a stoichiometric amount in almost all of organic reactions. Accordingly, if catalytic amounts of indium can be used in organic reactions, its usefulness and versatility should remarkably be increased. Recently, aqueous allylation reactions using a catalytic amount of InCl_3 ³ and indium-catalyzed allylation reaction were reported.⁴ Despite the recent progress, there is still strong need for various and efficient indium-catalyzed organic reactions. Although the transition-metal catalyzed cross-couplings are one of the most straightforward methods for C-C bond formation,⁵ cross-couplings catalyzed by cooperative indium and palladium are to date unknown.⁶ We describe herein cooperative indium and palladium-catalyzed allyl cross-coupling reactions with manganese (Scheme 1).



Scheme 1. Cooperative catalysis by indium and palladium for the allyl cross-coupling reaction.

First, the reaction of allylindium generated *in situ* from indium and allyl iodide with 1-halonaphthalene was examined (Table 1). The reaction of **1** (1 equiv.) with allyl iodide (1.5 equiv.), In (20 mol%) and Mn (3 equiv.) in the presence of 3 mol% of $(\text{Ph}_3\text{P})_4\text{Pd}$ and LiCl (3 equiv.) produced **4** (20%), **5** (55%) and **6** (15%) in DMF at 100 °C under a nitrogen atmosphere (entry 11).



The use of **2** gave **4** and **5** in 35% and 50% yields, respectively and formation of **6** was restrained (entry 5). Addition of allyl iodide dropwisely over 4 h did not effect on

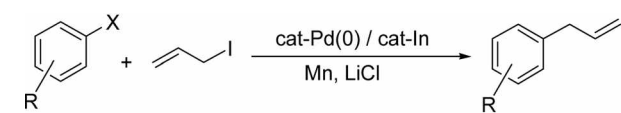
the reaction. The compound **4** and **5** was obtained in 10% and 15% yields, respectively, in dropwise of **2** over 4 h. The compound **3** did not give the desired product. In case of aluminum (3 equiv.) and zinc (3 equiv.), the compound **4** was produced in 20% yields (entries 3 and 4). Among the ligands (1,2-(Ph_2P)benzene, (*o*-Tol)₃P, Dppe, Dppf, XantPhos, DPPP, DPEphos and (2-Furyl)₃P) tested, Cy_3P gave the best results. DMF was the best solvent among several reaction media. Among the additives (LiX, K_2CO_3 , K_3PO_4 , CsF and *n*- Bu_4NX) screened, LiCl gave the best results. The addition of InCl_3 (5 mol%), InCl (20 mol%) and InI (20 mol%) did not increase the yield. The use of manganese (2 equiv.) gave **4** in 40% yield (entry 9), but the yield decreased to 20% without manganese (entry 10). These results indicate that indium salt **13** generated through transmetallation was reduced to In(0) by manganese and subsequently reacted with allyl iodide to produce allylindium. The best results were obtained with 1-bromonaphthalene (1 equiv.) and allyl iodide (1.5 equiv.) in the presence of 3 mol% $\text{Pd}_2\text{dba}_3\text{CHCl}_3$ /20 mol% Cy_3P , indium (20 mol%), manganese (3 equiv.) and LiCl (3 equiv.) in DMF at 100 °C under a nitrogen

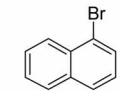
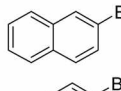
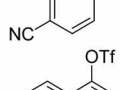
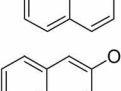
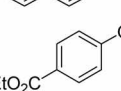
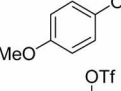
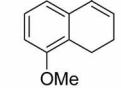
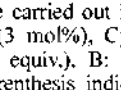
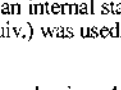
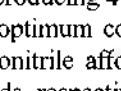
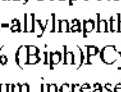
Table 1. Reaction optimization^a

Entry	X	M	Ligand ^b	Conversion (%) ^c	Yield (%) ^c
1	Br	Mn	Cy_3P	>98	55(20)
2	I	Mn	Cy_3P	>95	15(60)
3	Br	Al	Cy_3P	>95	20(50)
4	Br	Zn	Cy_3P	>95	20(50)
5 ^d	Br	Mn	–	80	35(50)
6	Br	Mn	Ph_3P	95	50(20)
7	Br	Mn	<i>tert</i> - Bu_3P	>98	10(85)
8 ^e	Br	Mn	Cy_3P	80	43(25)
9 ^f	Br	Mn	Cy_3P	>98	40(55)
10	Br	–	Cy_3P	>98	20
11 ^d	I	Mn	–	>95	20(55)(15) ^g

^aReactions were carried out with allyl iodide (1.5 equiv.), In (20 mol%), and M (3 equiv.) in the presence of $\text{Pd}_2\text{dba}_3\text{CHCl}_3$ (3 mol%) and LiCl (3 equiv.) in DMF (0.2 M) at 100 °C for 20 h. ^bLigand (20 mol%) was used. ^cGC yield using $\text{C}_{14}\text{H}_{30}$ as an internal standard. Numbers in parenthesis indicate yield **5**. ^d $(\text{Ph}_3\text{P})_4\text{Pd}$ (3 mol%) was used. ^eTHF was used as a solvent. ^fMn (2 equiv.) was used. ^g**6**.

[†]This paper is dedicated to Professor Sang Chul Shim on the occasion of his honorable retirement.

Table 2. Cooperative catalysis by indium and palladium with manganese for the allyl cross-coupling reactions^a


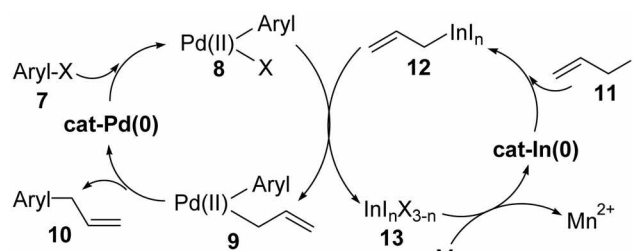
Entry	Electrophile	Condition ^b	Yield (%) ^c
1		A	48(55) ^d (20)
2		A	40(32)
3		A	46(28)
4		B	48(8)
5		B	46(8)
6 ^e			54(11)
7 ^f			44
8		B	52(12)
9 ^e			71(16)
10		B	42(14)
11			49(17)

^aReactions were carried out in DMF (0.2 M) at 100 °C for 20 h. ^bA: Pd-dba₃ClCHCl₃ (3 mol%), Cy₃P (20 mol%), LiCl (3 equiv.), In (20 mol%), Mn (3 equiv.). B: (Biph)PCy₂ (20 mol%). ^cIsolated yield. Numbers in parenthesis indicate the GC yield of reduction products using C₁₄H₃₀ as an internal standard. ^dGC yield of **4**. ^eIn (30 mol%) was used. ^fMn (4 equiv.) was used.

atmosphere, producing **4** in 55% yield (entry 1).

Under the optimum conditions, 2-bromonaphthalene and 4-bromobenzonitrile afforded the desired products in 40% and 46% yields, respectively (Table 2). In case of triflate of 2-naphthol, 2-allylnaphthalene was produced in 46% yield with 20 mol% (Biph)PCy₂ (entry 5). Although the use of 30 mol% of indium increased the product yield in 54%, the use of manganese (4 equiv.) decreased yield (44%) (entries 6 and 7). Triflate of 1-naphthol gave the **4** in 48% yield (entry 4). Reaction of triflate of ethyl 4-hydroxybenzoate with allylindium afforded the desired product in 52% yield (entry 8). Allyl cross-coupling product was produced in 71% yield with indium (30 mol%) (entry 9). However, triflate of 4-hydroxyphenyl methyl ketone yielded allyl alcohol in 70% yield, indicating that ketone group is more reactive than triflate for allylindium (eq. 1). Subjecting triflate of 4-hydroxyanisole to the optimum conditions gave 4-allylanisole in 42% yield (entry 10). Vinyl triflate afforded the desired product in 49% yield (entry 11).

A plausible reaction mechanism is shown in Scheme 2. The initially formed σ -Pd(II) complex **8** undergoes transmetalation by allylindium **12** to give **9** and indium salt **13**.

**Scheme 2.** A plausible reaction mechanism.

Then, the compound **9** is subjected to reductive elimination to yield allyl cross-coupling products **10**. Although we don't know the exact valence of indium in **13**, we believe that manganese reduce **13** to regenerate In(0) because use of manganese increase obviously yield of coupling product.⁷

In summary, cooperative indium and palladium-catalyzed allyl cross-coupling reactions were demonstrated. Allyl-indium generated *in situ* from allyl iodide, catalytic amount of indium, and manganese gave allyl cross-coupling products in moderate yields. This is the first example of cooperative catalysis by indium and palladium for cross-coupling reactions.

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